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# THE DOCTORAL RESEARCH ABSTRACTS

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**Title :** CHEMICAL CONSTITUENTS OF *Croton laevifolius* BLUME BARK

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Phytochemical investigation on the bark of Malaysian Croton laevifolius Blume (Euphorbiaceae) was carried out with an intention of isolating and identifying its chemical constituents. The bark was successively extracted with the non polar (hexane), medium polar (dichloromethane) and polar (methanol) organic solvents. These extracts were evaluated for cytotoxicity, anti-inflammatory and antidiabetic activities. The hexane extract showed potential cytotoxicity against MCF-7 cell line and mild cytotoxicity against A549, WRL-68, PC-3 and A375 cells while dichloromethane (DCM) extract indicated mild and selective activity against A549 and A375 only. The hexane and DCM extracts were subjected to isolation and purification using various chromatographic techniques such as Medium Pressure Liquid Chromatography (MPLC), Radial Chromatography (RC) and Recycling Preparative High Performance Liquid Chromatography (RHPLC). Structures of the chemical compounds were elucidated using various spectroscopic techniques such as UV, IR, 1D-NMR (1H, 13C, DEPT and APT), 2D-NMR (COSY, HSQC, HMBC and NOESY) and mass spectrometry. This study has led to the isolation of fourteen compounds, in which seven new and one known clerodane type diterpene named crovatin, as well as one eudesmane-type sesquiterpene named crytomeridiol were isolated from the DCM extract. This is the first occurrence of cryptomeridiol in Croton species. The new diterpenes were deduced as laevifin A, laevifin B, laevifin C, laevifin D, laevifin E, laevifin F and laevifin G. Subsequently, the hexane extract yielded laevifin B, three oleanane triterpenes: β-amyrin, β-amyrone and acetyl aleuritolic acid; one steroid (β-sitostenone) and one flavonoid named pachypodol. The absolute configurations of the isolated clerodane diterpenes were established using Electronic Circular Dichroism (ECD) technique where the experimental ECD profiles of the compounds were compared to that of TDDFT calculated spectra. The absolute configuration of these diterpenes has led to the postulation of their biosynthetic pathways via a biosynthetic study. Selected compounds of sufficient quantity were further evaluated for their toxicity against MCF-7 and A375 cell lines and anti-inflammatory activity by LPS-induced NF-κB translocation inhibition in RAW 264.7 cells. The isolated compounds of sufficient amount were further tested for cytotoxicity. Compounds laevifins A, B and F displayed fair cytotoxicity with IC50 values of 115, 102 and 106 μM respectively while β-amyrone and β-sitostenone showed medium cytotoxicity against MCF-7 cell line with IC50 values of 73 and 94 μM respectively. In addition, β-amyrin and acetyl aleuritolic acid showed weak activities; sharing IC50 values of 115 μg/mL. Laevifin E, acetyl aleuritolic acid and β-sitostenone showed weak activities against A375 cell line with IC50 values of 152, 103 and 124 μM respectively. In anti-inflammatory evaluation, the hexane extract showed weak activity where compounds β-amyrin and acetyl aleuritolic acid of the hexane extract showed good anti-inflammatory activity at the concentration of 50 μg/mL.